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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/033,629	12/28/2001	Richard J. Deckelbaum	0575/61238-A/JPW/BJA	9269

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EXAMINER	
DAVIS, RUTH A	

ART UNIT	PAPER NUMBER
1651	

DATE MAILED: 11/28/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application N .	Applicant(s)	
	10/033,629	DECKELBAUM ET AL.	
	Examiner	Art Unit	
	Ruth A. Davis	1651	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 September 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-3 and 10-30* is/are pending in the application.

4a) Of the above claim(s) *12-14,18-23 and 26-30* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-3,10-11,15-17,24-25* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. §§ 119 and 120

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

13)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application) since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

a) ☐ The translation of the foreign language provisional application has been received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121 since a specific reference was included in the first sentence of the specification or in an Application Data Sheet. 37 CFR 1.78.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Applicant's amendment and response filed September 15, 2003 has been received and entered into the case. Claims 4 – 9 are canceled; claims 12 – 14, 18 – 23 and 26 – 30 are withdrawn from consideration; claims 1 - 3, 10 – 11, 15 – 17 and 24 25 have been considered on the merits. All arguments have been fully considered.

Claim Rejections - 35 USC § 112

1. Rejections under 35 U.S.C. 112, second paragraph, have been withdrawn due to amendment.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claims 1 – 3, 11 and 24 – 25 stand rejected under 35 U.S.C. 102(b) as being anticipated by Treskova.

Applicant claims an emulsion consisting of a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride; the composition is delivered to extrahepatic

tissue; the omega 3 triglyceride effects delivery of the pharmaceutical agent; and the composition has 80% of the particles with a diameter of 150 – 350 nm. Applicant additionally claims an emulsion consisting of a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions consisting of 3H-CE, emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract).

The reference anticipates the claimed subject matter.

Applicant argues that Treskova does not teach the emulsion with therapeutically effective amounts of a pharmaceutical agent.

However, this argument fails to persuade because Applicant specifically teaches examples of pharmaceutical agents to include compounds that are not water soluble and radioactive tracers (specification p.22, example 1). Treskova specifically teaches 3H-CE in the emulsion which is both water insoluble and a radioactive tracer. As such, the claims stand rejected as being anticipated by Treskova.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(c), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1 – 3, 10 – 11 and 24 – 25 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pscherer, Wretlind or Boll.

Applicant claims an emulsion consisting of a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride; the composition is delivered to extrahepatic tissue; the omega 3 triglyceride effects delivery of the pharmaceutical agent; and the composition has more than 80% or the particles with a diameter of 30 – 150nm or 150 – 350 nm. Applicant additionally claims an emulsion consisting of a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Pscherer teaches lipid emulsions comprising MCT, LCT, omega 3 triglycerides in the form of fish oil, emulsifiers and vitamin E (a pharmaceutical agent) (col.2 – 4). The particle sizes are less than 0.5 micrometers (col.5 line 6-7).

Wretlind teaches emulsion compositions for delivering therapeutics (abstract), the composition comprising fish oil (which intrinsically contains omega 3 triglycerides), emulsifiers, pharmaceutical agents and LCT with particle sizes of 0.005 – 0.5 microns (5 – 500 nm) (col.4).

Boll teaches lipid emulsions containing omega 3 fatty acids as fish oil, an emulsifier, MCT and tocopherols (a pharmaceutical agent) for endotracheal treatment (abstract).

Although the references do not teach the component amounts are predetermined to delivery pharmaceutical agents to predetermined tissues, such activity is intrinsic to the pharmaceutical compositions. In addition, the references do not teach the claimed particle sizes. However, at the time of the claimed invention, it would have been well within the purview of one of ordinary skill in the art to optimize such parameters as a matter of routine experimentation. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the emulsion particle size of the reference compositions with a reasonable expectation for successfully obtaining effective pharmaceutical compositions. Finally, while the references teach the compositions to include additional components, it would have been well within the purview of one of ordinary skill in the art to omit components where their functions are not desired.

Applicant argues that the references contain additional ingredients and therefore do not anticipate the claims.

However, this argument fails to persuade because while the reference compositions may contain additives for preservation, flavor or other functions, it would certainly have been obvious to one of ordinary skill in the art to omit such components where such functions are not desired or required. Therefore, the claims are rejected for these reasons, and those made above.

7. Claims 1 – 3, 10 – 11 and 24 – 25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Treskova.

Applicant claims an emulsion consisting of a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride; the composition is delivered to extrahepatic tissue; the omega 3 triglyceride effects delivery of the pharmaceutical agent; and the composition has 80% of the particles with a diameter of 30 – 150 nm or 150 – 350 nm. Applicant additionally claims an emulsion consisting of a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions consisting of 3H-CE, emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract).

Althouh Treskova does not teach the emulsions with particle sizes of 30 – 150 nm, it would have been well within the purview of one of ordinary skill in the art to optimize particle size as a matter of routine experimentation (see other cited references for support). Therefore, at

the time of the claimed invention, one of ordinary skill in the art would have been motivated by routine practice to optimize the emulsion particle size of Treskova with a reasonable expectation for successfully obtaining an effective emulsion composition.

Applicant argues that Treskova does not teach the emulsion with therapeutically effective amounts of a pharmaceutical agent and therefore does not anticipate the claims.

However, this argument fails to persuade because Applicant specifically teaches examples of pharmaceutical agents to include compounds that are not water soluble and radioactive tracers (specification p.22, example 1). Treskova specifically teaches 3H-CE in the emulsion which is both water insoluble and a radioactive tracer. As such, the claims stand rejected as being anticipated by Treskova.

8. Claims 1 – 3, 10 – 11, 15 – 17 and 24 – 25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Treskova and Counsell.

Applicant claims an emulsion consisting of a pharmaceutical agent, fish oil and emulsifier. The fish oil is an omega 3 triglyceride; the composition is delivered to extrahepatic tissue; the omega 3 triglyceride effects delivery of the pharmaceutical agent; and the composition has 80% of the particles with a diameter of 30 150 nm or 150 – 350 nm. Applicant claims an emulsion comprising a pharmaceutical agent, triglyceride, emulsifier and ligand, wherein the triglyceride delivers the pharmaceutical agent to a tissue, and the ligand effects delivery of the agent. The ligand is apolipoprotein E, specifically human apolipoprotein E or homologs thereof

differing by less that 3 amino acids and having activity of human apolipoprotein E. Finally, applicant claims an emulsion consisting of a pharmaceutical agent, triglyceride and emulsifier wherein the triglyceride is a medium or long chain triglyceride.

Treskova teaches therapeutic (pharmaceutical, thus contain a pharmaceutical agent) emulsions consisting of 3H-CE, emulsifiers, long chain triglycerides (LCT), medium chain triglycerides (MCT), and omega 3 fatty acids (triglycerides) in the form of fish oil, with emulsion particle sizes of about 300 nm (p.254). Treskova teaches the composition is such that omega 3 triglyceride increases delivery of the agent to extrahepatic tissues (abstract).

Counsell teaches emulsions for hepatic tissue selective delivery of pharmaceuticals (abstract), comprising a lipophilic core and emulsifier (col.5 line 50-59). The core may contain LCT and fish oils (col.5 line 66 – col.6 line 9, col.11), and the emulsion particle size is 50 – 200 nm (abstract).

The above references do not specifically teach the emulsions comprising the ligand apolipoprotein E, or homologs thereof. However, Treskova does suggest that uptake of the triglycerides is increased in the presence of apolipoprotein E (p.257). In addition, Counsell teaches that the emulsion must associate with apolipoprotein E to make it hepatocyte specific (col.4-5). At the time of the claimed invention, one of ordinary skill in the art would certainly have been motivated by the teachings of Treskova and Counsell to include apolipoprotein E, or homologs thereof, in the disclosed compositions for it's specificity to hepatic and extrahepatic tissues, and for the disclosed effect of increasing triglyceride uptake. Moreover, at the time of the claimed invention, one of ordinary skill in the art would have been motivated by Treskova and Counsell to include apoplipoprotein E or homologs thereof in the compositions with a

reasonable expectation for successfully obtaining an emulsion for delivering an agent to extrahepatic tissue.

Applicant argues the references do not teach the compositions with therapeutic agents or effects and that they do not teach or suggest the compositions with apolipoprotein E.

However, these arguments fail to persuade because both Treskova and Counsell expressly teach the triglyceride compositions are more efficacious when combines or associated with apolipoprotein E. These teaching would certainly motivate one of ordinary skill in the art to include apolipoprotein E in the reference compositions. In addition, Applicant specifically identifies examples of pharmaceutical agents to include compounds that are not water soluble and radioactive tracers (specification p.22, example 1). Treskova teaches 3H-CE in the emulsion which is both water insoluble and a radioactive tracer while Counsell teaches pharmaceuticals in the compositions (abstract). Therefore, for these reasons and those above, the claims remain rejected.

Conclusion

9. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO

MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ruth A. Davis whose telephone number is 703-308-6310. The examiner can normally be reached on M-H (7:00-4:30); altn. F (7:00-3:30).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Wityshyn can be reached on 703-308-0196. The fax phone number for the organization where this application or proceeding is assigned is 703-308-4242.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Ruth A. Davis; rad
November 25, 2003.

LEON B. LANKFORD, JR.
PRIMARY EXAMINER